

## **Supplementary information**

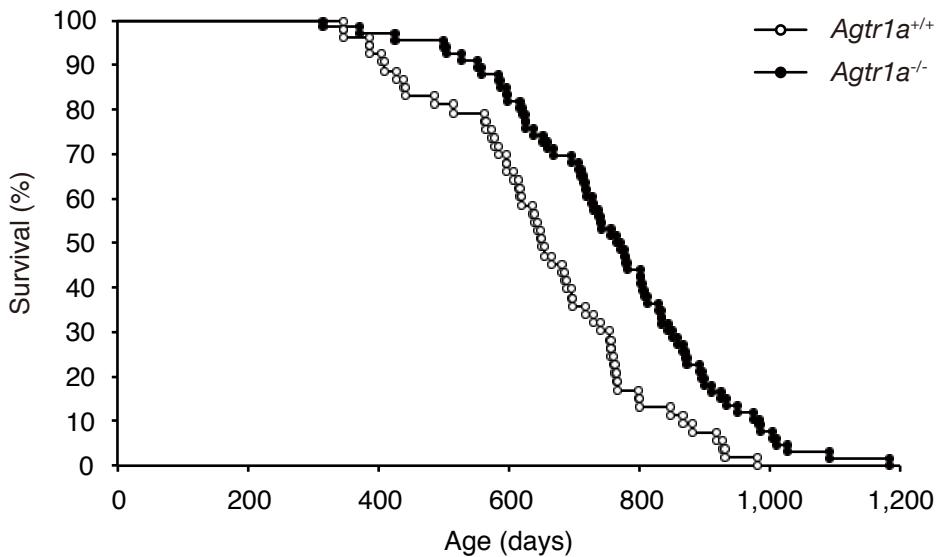
### **Angiotensin II receptor blockade promotes repair of skeletal muscle through down-regulation of aging-promoting C1q expression**

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**Supplementary Table 1. Heart rates and blood pressures of irbesartan- or vehicle-treated mice**

	0 d		14 d	
	Vehicle	Irbesartan	Vehicle	Irbesartan
Number	6	6	6	6
Heart rate (bpm)	640.2 $\pm$ 33.5	674.8 $\pm$ 15.2	695.5 $\pm$ 16.9	688.3 $\pm$ 11.7
SBP (mmHg)	102.2 $\pm$ 0.9	101.2 $\pm$ 0.8	102.7 $\pm$ 0.7	102.8 $\pm$ 2.0
DBP (mmHg)	59.7 $\pm$ 3.9	56.8 $\pm$ 5.1	65.0 $\pm$ 1.5	61.5 $\pm$ 5.9
MBP (mmHg)	71.8 $\pm$ 1.8	71.4 $\pm$ 2.9	76.6 $\pm$ 1.7	73.8 $\pm$ 3.4

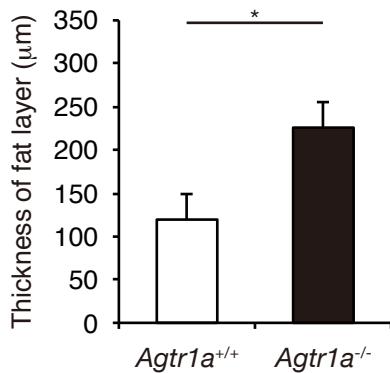
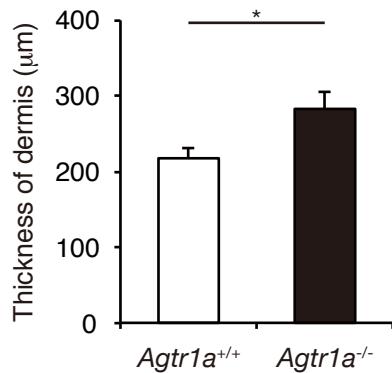
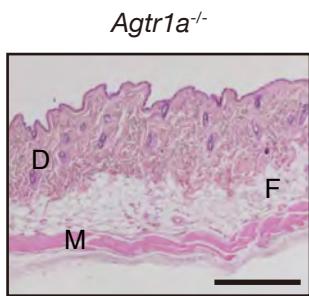
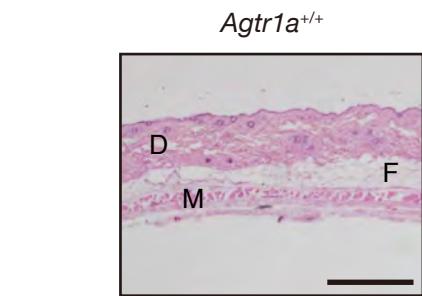
Values are mean  $\pm$  SEM. SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure.



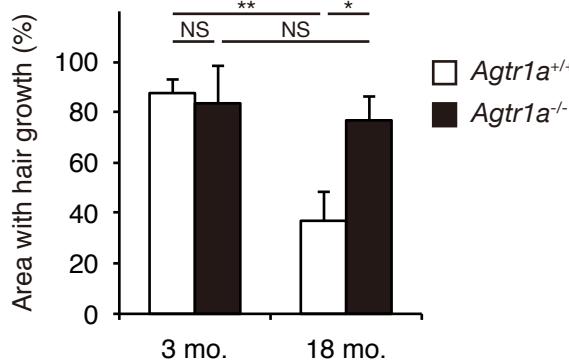
**Supplementary Figure 1. Genetic disruption of *Agtr1a* extended life span in mice.**

Kaplan-Meier survival curves of *Agtr1a*<sup>-/-</sup> ( $n = 66$ ) and *Agtr1a*<sup>+/+</sup> ( $n = 55$ ) mice. The average life span of *Agtr1a*<sup>-/-</sup> and *Agtr1a*<sup>+/+</sup> mice was  $760.0 \pm 20.9$  and  $651.8 \pm 21.7$  days, respectively ( $P < 0.05$ ).

a.



b.

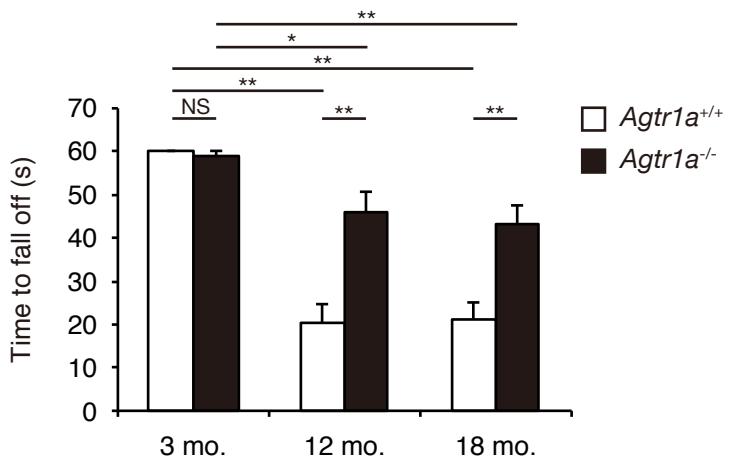


### Supplementary Figure 2. Aging-related changes in the skin of $\text{Agtr1a}^{-/-}$ and $\text{Agtr1a}^{+/+}$ mice.

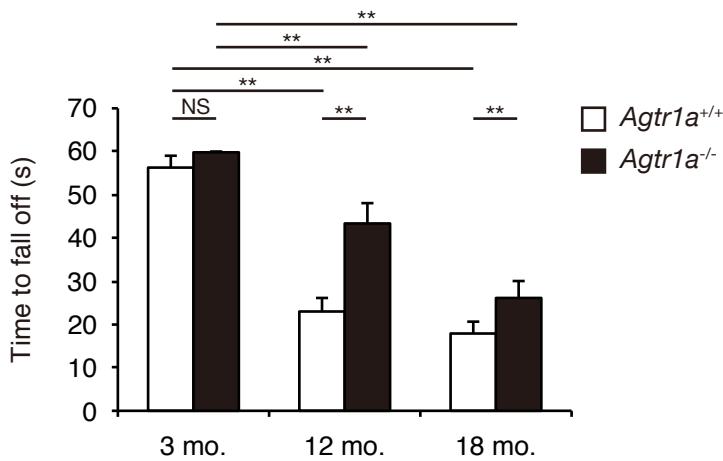
(a) Representative images of hematoxylin-eosin staining (upper panels) and the thickness of dermis and fat layer (lower panels,  $n = 8$  in each group) in 21-month-old  $\text{Agtr1a}^{-/-}$  and  $\text{Agtr1a}^{+/+}$  mice. F, fat; D, dermis; M, muscularis. \* $P < 0.05$ . Scale bars, 500  $\mu\text{m}$ .

(b) Representative photos of 18-month-old  $\text{Agtr1a}^{-/-}$  and  $\text{Agtr1a}^{+/+}$  mice at 28 d after shaving of hair from a 2  $\text{cm}^2$  dorsal area (upper panels) and the fraction of hair growth in 3- and 18-month-old  $\text{Agtr1a}^{-/-}$  and  $\text{Agtr1a}^{+/+}$  mice (lower panel) (3-month-old  $\text{Agtr1a}^{+/+}$  mice,  $n = 5$ ; 3-month-old  $\text{Agtr1a}^{-/-}$  mice,  $n = 6$ ; 18-month-old  $\text{Agtr1a}^{+/+}$  mice,  $n = 9$ ; 18-month-old  $\text{Agtr1a}^{-/-}$  mice,  $n = 11$ ). \* $P < 0.05$ , \*\* $P < 0.01$ , NS, not significant.

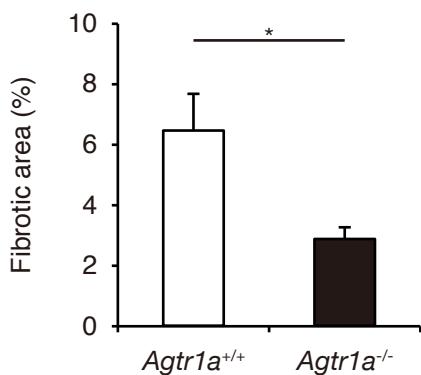
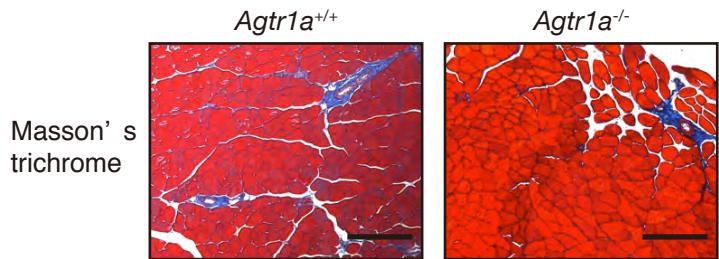
a.



b.

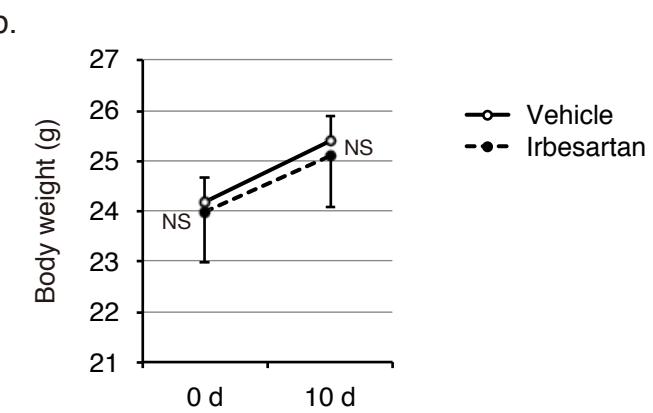
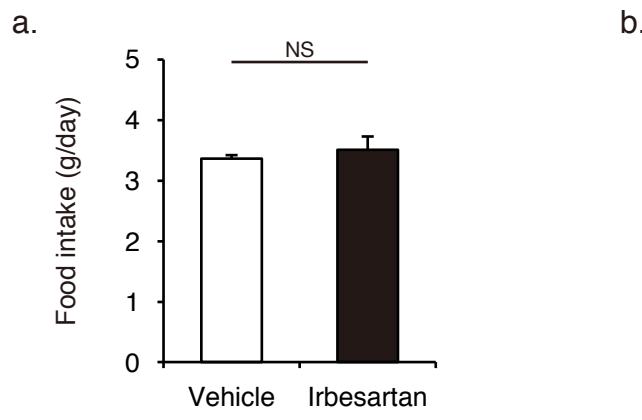


c.



**Supplementary Figure 3. Aging-related changes in the skeletal muscle structure and function of *Agtr1a*<sup>-/-</sup> and *Agtr1a*<sup>+/+</sup> mice.**

- (a) The comparison of motor balance using a vertical pole test in 3-, 12-, and 18-month-old *Agtr1a*<sup>-/-</sup> and *Agtr1a*<sup>+/+</sup> mice (3-month-old *Agtr1a*<sup>+/+</sup> mice,  $n = 7$ ; 3-month-old *Agtr1a*<sup>-/-</sup> mice,  $n = 7$ ; 12-month-old *Agtr1a*<sup>+/+</sup> mice,  $n = 14$ ; 12-month-old *Agtr1a*<sup>-/-</sup> mice,  $n = 12$ ; 18-month-old *Agtr1a*<sup>+/+</sup> mice,  $n = 17$ ; 18-month-old *Agtr1a*<sup>-/-</sup> mice,  $n = 17$ ). \* $P < 0.05$ , \*\* $P < 0.01$ , NS, not significant.
- (b) The comparison of muscular strength, tone, and equilibrium using a hanging wire test in 3-, 12-, and 18-month-old *Agtr1a*<sup>-/-</sup> and *Agtr1a*<sup>+/+</sup> mice (3-month-old *Agtr1a*<sup>+/+</sup> mice,  $n = 7$ ; 3-month-old *Agtr1a*<sup>-/-</sup> mice,  $n = 7$ ; 12-month-old *Agtr1a*<sup>+/+</sup> mice,  $n = 14$ ; 12-month-old *Agtr1a*<sup>-/-</sup> mice,  $n = 12$ ; 18-month-old *Agtr1a*<sup>+/+</sup> mice,  $n = 17$ ; 18-month-old *Agtr1a*<sup>-/-</sup> mice,  $n = 17$ ). \*\* $P < 0.01$ , NS, not significant.
- (c) Histological sections with Masson' s trichrome staining of TA muscles in approximately 24-month-old *Agtr1a*<sup>-/-</sup> and *Agtr1a*<sup>+/+</sup> mice. Right panel indicates the percent area of fibrosis in Masson' s trichrome staining of TA muscles (*Agtr1a*<sup>+/+</sup> mice,  $n = 6$ ; *Agtr1a*<sup>-/-</sup> mice,  $n = 6$ ). Scale bars, 200  $\mu$ m, \* $P < 0.05$ .



**Supplementary Figure 4. Peripherally administered irbesartan had no effect on food intake and body weight.**

- (a) Daily food intake of irbesartan- or vehicle-treated mice ( $n = 5$ , in each group). NS, not significant.
- (b) Body weight of mice at 0 d and 10 d after treatment with irbesartan or vehicle ( $n = 5$ , in each group). NS, not significant.